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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/663,570
Filing Date: September 15, 2003
Appellant(s): MONGEON ET AL.

Jessica Kwak
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 6/18/2010 appealing from the Office action mailed 2/19/2010.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 21-24, 26, 29-33, 35-42, and 46-54 are pending.

Claims 21-24, 26, 29-33, 35-42, and 46-54 are rejected.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is substantially correct. On page 5, "claim 1" should read --claim 21--.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the

subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

4,819,662	Heil, Jr. et al.	4-1989
6,151,525	Soykan et al.	11-2000
2004/0158289	Girouard et al.	8-2004

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Pending rejection under 35 U.S.C. 103(a) in view of Soykan, Heil, and Girouard:

Claim	Limitation	Disclosure in prior art	Reason to modify
21	A medical lead comprising:	Soykan's medical lead system is generally described at column 13, lines 38-54.	
	A lead body;	Soykan's lead body is described at, e.g., col. 13, lines 49-54.	
	A porous electrode mounted on a lead body to deliver electrical stimulation to a stimulation site within a patient; and	Heil teaches a system having a porous electrode mounted on a lead body as element 150 in Figure 7.	To provide controlled release of pharmacological agents at the site of electrical therapy.
	A genetic material that causes expression of at least one of a connexin or a gap junction by the tissue at the stimulation site,	Girouard teaches causing expression of connexin by the treated tissue at the stimulation site by application of a genetic material at paragraph 0146.	To repair damaged heart tissue.

	wherein the expression of the at least one of the connexin or gap junction by the tissue at the stimulation site increases the conductivity of the tissue.		
	A chamber body that defines a chamber, the chamber containing a polymeric matrix that absorbs genetic material and elutes the genetic material to tissue at the stimulation site via the porous electrode,	Soykan discloses that the genetic material is eluted using a silicone polymeric matrix at column 11, line 49, and Heil discloses a chamber body shown as element 168 in Figure 7 that contains a polymeric (silicone) matrix 170. This is further described by Heil at column 4, lines 45-49 and column 6, lines 49-66.	To provide controlled release of pharmacological agents at the site of electrical therapy.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-24, 26, 29-33, 35-42, and 46-54 are rejected under 35 U.S.C. 103(a) as obvious over Soykan in view of Heil, Jr. et al. (US 4,819,662, hereinafter “Heil”) and Girouard et al. (US 2004/0158289, hereinafter “Girouard”).

In regards to claims 21, 22, 24, 29, 35, 46, 47, 49, 51, and 54, Soykan discloses a method/system comprising a lead for delivering electrical stimulation to tissue (col. 13, line 38) and eluting genetic material from a polymeric matrix (col. 11, line 1) comprising extracellular collagen (col. 11, lines 46-60 -- the polymer is further disclosed as "biodegradable" at line 46) to cause transgenic expression that increases the conductivity at the stimulation site. Increasing the contractile ability of the stimulation area (from cells that do not contract at all, per column 1, lines 57-58, to cells that contract, per the abstract of the disclosure) necessarily increases the conductivity because non-contractile cells do not have the membrane proteins that allow for cell contraction, while contractile cells do have these proteins. This necessary feature of these cells means that the conductivity is increased in the region of these new cells. Further, this increase in contractile ability necessarily creates some preferential conduction pathway between the stimulation site and at least one of a bundle of His or a Purkinje fiber because the applied pulse or propagating action potential must follow some preferred path created by the improved conductivity of the treated region of the heart. For example, referring to Figure 1, after treatment, action potentials generated in the newly treated region will flow through a different path than when the tissue was not

fully-functioning contractile heart tissue. Soykan does not disclose a separable chamber that elutes material from a porous electrode or that the genetic material causes expression of connexin-43 or a gap-junction. Heil teaches providing a lead with a removable chamber that elutes substances through a porous electrode for the purpose of providing controlled release of pharmacological agents at the site of electrical therapy (abstract, Fig. 7). Further, Girouard teaches providing a cardiac therapy comprising causing expression of connexin-43 for the purpose of repairing damaged heart tissue (par. 0146). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Soykan's invention by providing a lead with a chamber that elutes substances through a porous electrode for the purpose of providing controlled release of pharmacological agents at the site of electrical therapy and providing a cardiac therapy comprising delivering connexin for the purpose of repairing damaged heart tissue.

In regards to claims 23, 37, and 48, the matrix is cross-linked (col. 11, lines 47 and 55). The level of cross-linking is inherently proportional to the release rate, and natural collagen is cross-linked.

In regards to claims 26 and 50, the delivery vector is a liposome (claim 7).

In regards to claims 32, the electrode is implantable (col. 13, line 49).

In regards to claims 33, the tissue is cardiac tissue (abstract).

In regards to claims 30, 31, 36, 38-42, 52, and 53, Soykan's modified invention discloses the essential features of the claimed invention, including using autologous

biological material (col. 5, line 67) that is incorporated just prior to delivery by swelling the hydrogel (col. 11, line 59), but does not disclose a freeze-dried (lyophilized) or frozen matrix, a genetic material that causes expression of a metalloproteinase, an anti-inflammatory agent comprising IkB, or an immunosuppressant agent, placing the matrix in the lead just before implantation, or soaking of the distal end of the lead in the genetic material. It is well known in the art to freeze-dry or freeze matrix to increase the shelf-life of the biologically active substance, to provide genetic materials that cause expression of a metalloproteinase, an anti-inflammatory agent comprising IkB, or an immunosuppressant agent to reduce rejection complications in a host patient, and to soak (or swell) matrix in genetic material before placement into the body (either before delivery, or right at delivery) to allow autologous biological substances to be implanted. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify Soykan's invention by freeze-drying or freezing matrix to provide the predictable result of increasing the shelf-life of the biologically active substance, to provide genetic materials that cause expression of a metalloproteinase, an anti-inflammatory agent comprising IkB, or an immunosuppressant agent to provide the predictable result of reducing rejection complications in a host patient and soaking matrix in genetic material before placement into the body to provide the predictable result of allowing autologous biological substances to be implanted.

(10) Response to Argument

CLAIMS 21-24, 26, AND 29-33

Appellant argued that the combination of Soykan, Heil, and Girouard under 35 U.S.C. 103(a) lacks a rational underpinning because an artisan of ordinary skill would not be motivated to apply Heil's lead configuration to Soykan's system to provide "controlled release of pharmacological agents at the site of electrical therapy" because Soykan's system already does this, as shown by Soykan's disclosure at column 11, lines 5-7 (indicating that the genetic material may be incorporated into a carrier, which may be an electrical stimulation device). However, Soykan is silent as to precisely where on or in the electrical stimulation device the carrier resides. Heil is provided as a teaching of one of many prior-art configurations wherein the therapeutic agent carrier is a porous electrode. Because of Soykan's silence concerning the *specific* location on the device for the carrier, the Examiner maintains the position that looking to prior art carrier configurations, such as Heil's, would require only ordinary skill in the art. The Examiner further maintains that an artisan of ordinary skill would be motivated to make this modification to provide the agent *at the site of electrical therapy*. Heil provides the therapeutic agent to, *e.g.*, "reduce the problem of acute stimulation threshold increase" and "counter[] chronic threshold increase" (col. 2, lines 35-40); both of which are phenomena associated with the electrode-body interface of the stimulation system. Soykan's genetic agent provides for increasing the contractility of cardiac tissue (abstract) and stimulating those very cells with the electrical stimulation system. The Examiner maintains the position that an artisan of ordinary skill would be motivated to modify Soykan's invention (disclosing agent delivery at an unspecified location on the electrical stimulator or catheter) by providing the agent at the site of electrical

stimulation, as taught by Heil, because the cells that are the target of the therapeutic agent are the same cells that are the target of the electrical therapy -- it follows that it is desirable to apply the agent at the electrode. Furthermore, while a teaching, suggestion, or motivation is sufficient to render the combination obvious, it is not necessary. *See KSR.* An alternative basis is a showing that the combination is a simple substitution of one known element for another to obtain predictable results. The Examiner maintains that the modification of Soykan's electrical stimulation device by providing the known lead structure of Heil would be an example of such "simple substitution" as the interchangability of leads and electrical stimulators is known in the art. Applicant further argued that substituting the specific delivery configuration of Heil for the generically-described delivery configuration of Soykan would be more than a "simple substitution" because a drug "may have different purposes and different properties" than the genetic material of Soykan. *See* page 6 of "Appeal Brief". While this may or may not be true, there is simply nothing in the record to indicate any actual difference between drug and genetic material warranting "secondary considerations" of non-obviousness. In other words, Applicant has set forth the possibility of "secondary considerations" existing without actually setting forth or establishing a factual basis for these considerations. Although it is possible that differences exist between drug and genetic material delivery, none of these differences have been set forth in the record. Different therapeutic effect does not speak to the ability of a mechanical delivery device to mechanically elute the substance. The examiner maintains that there is a reasonable expectation of success of the combination because both teachings provide exemplary

embodiments of eluting the genetic material and/or drug with, *e.g.*, a silicone matrix (*see* Soykan at col. 11, lines 43-52 and Heil at col. 45, lines 45-49). It is noted that Appellant has not disclosed that diffusion of genetic material through the porous electrode requires more than mere fluid communication with the genetic material (*see, e.g.*, paragraph 0030 of Appellant's disclosure).

Appellant further argued that the combination of Girouard is also erroneous because the Girouard's genetic material is applied to cells *in vitro*, and the cells are later administered to the patient, while Soykan provides genetic material directly to the patient's cells within the body. Referring to paragraph 0044 and Figures 1A and 1C, Girouard recognizes that the vectors may be applied either *in vitro* or *in vivo,* and does not require an *in vitro* conditioning step. Please note that the flowcharts of Figures 1A and 1C clearly omit the step of *in vitro* conditioning to which Appelant relies for the proposition that Girouard *requires* this step. The Examiner maintains that an artisan of ordinary skill could have predictably applied Girouard's teaching of providing genetic material that causes the expression of connexin to Soykan's system. Soykan's system utilizes, *e.g.*, a viral or liposome vector incorporated into a carrier (col. 11, lines 1-7) to create or repopulate contractile cells. Girouard has identified genetic material that causes the expression of connexin, identified that this genetic material is useful for improving the contractility of heart tissue, has isolated this genetic material in a delivery vector, and discloses applying electrical energy at the site of delivery after delivery (*e.g.*, Fig. 1A). Appellant has provided no evidence that this material isolated in vector form is somehow unusable *in vivo*, and Girouard discloses the contrary (par. 0044). Moreover,

Girouard's disclosure that the material is isolated and provided in a vector similar to those used by Soykan, and that the vector is usable *in vivo* indicate that an artisan of ordinary skill could have predictably substituted Girouard's genetic material-containing vector for the genetic material-containing vector of Soykan's carrier. Applying Girouards's vector to Soykan's system would not require a modification to Girouard, and would render no more than predictable results.

CLAIM 46

Appellant argued that Soykan's disclosure of converting non-contractile cells to contractile cells does not create a "preferential conduction pathway" because the new contractile cells may create a path that is the same or less preferred to another pathway. Appellant further reasoned that, although the conversion of non-contractile cells to contractile cells may improve the conduction pathway compared to the pathway that existed prior to the conversion, this does not necessarily result in a pathway that is more preferred over other pathways between the stimulation site and the bundle of His or Purkinje fiber. However, the claim does not require the optimum, shortest (or even shorter) pathway, and does not indicate who or what "prefers" the new conduction pathway. As the current (or action potential) necessarily follows a new path because of the new contractile tissue, this path is "preferred" by the current or action potential to the pre-therapy path. Further, because this genetic therapy has converted surrounding cells to a more contractile state, this conduction pathway is shorter than the pathway existing before the therapy. Although one possible meaning of "preferred" is shorter or

faster or in some other may more optimal than other spatial pathways, another possible and reasonable reading of "preferred" is a shorter or faster or more optimal temporal pathway (*i.e.*, "preferred to the previous one"). Most importantly, claim 46 is an apparatus claim with a functional recitation of the genetic material. There is no method step of applying the genetic material to a certain location to create a preferred pathway, but merely a genetic material *adapted to* create a preferential conduction pathway. In other words, the genetic material need only be capable of creating a preferred conduction pathway. Because Soykan's genetic material increases conductivity, it is capable of creating any desired conduction pathway, depending on the site of application by the clinician. The "adaptation" of the genetic material is the ability to increase conductivity of heart tissue, and Soykan does this. Again, it is stressed that claim 46 is not a method claim requiring any sort of step drawn to applying the genetic material to a certain specific location.

CLAIMS 35-42

The reasoning applied to claim 21 likewise applies to these claims.

CLAIMS 47-54

The reasoning applied to claim 21 likewise applies to these claims.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully Submitted,

/Michael Kahelin/

Examiner, Art Unit 3762

Conferees:

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RQAS -3700